

CLAIMS

What is claimed is:

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1. An isolated nucleic acid encoding a mammalian immunodeficiency virus glycoprotein (gp) 120 polypeptide, or a mutant, derivative, or fragment thereof, wherein said gp120 polypeptide comprises a deletion of hypervariable loop 3 (V3), and further comprises a compensatory mutation.

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2. The isolated nucleic acid of claim 1, wherein said mammalian immunodeficiency virus is selected from the group consisting of a simian immunodeficiency virus (SIV), a human immunodeficiency virus type 1 (HIV-1), and a human immunodeficiency virus type 2 (HIV-2).

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3. The isolated nucleic acid of claim 2, wherein said mammalian immunodeficiency virus is HIV-2.

4. The isolated nucleic acid of claim 3, wherein said deletion of V3 is selected from the group consisting of a deletion of from about amino acid residue number 303 to amino acid residue number 324 ($\Delta V3(6,6)$) relative to the amino acid sequence of HIV-2/vcp gp120 as provided in SEQ ID NO:5, and a deletion from about amino acid residue number 298 to amino acid residue number 331 ($\Delta V3(1,1)$) relative to the amino acid sequence of HIV-2/vcp gp120 as provided in SEQ ID NO:5.

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5. The isolated nucleic acid of claim 3, wherein said deletion of V3 is a deletion from about nucleotide number 894 to nucleotide number 1032 ($\Delta V3(1,1)$) encoding from about amino acid residue number 298 to amino acid residue number 331 relative to the amino acid sequence of HIV-2/vcp gp120 as provided in SEQ ID NO:5.

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6. The isolated nucleic acid of claim 4, wherein said gp120 further comprises a deletion of the V1/V2 region.

7. The isolated nucleic acid of claim 1, wherein said compensatory mutation is at least one mutation selected from the group consisting of an amino acid substitution from isoleucine to valine at amino acid residue number 55, an amino acid substitution from asparagine to aspartic acid at amino acid residue number 79, an amino acid substitution from phenylalanine to serine at amino acid residue number 94, an amino acid substitution from aspartic acid to glycine at amino acid residue number 142, an amino acid substitution from threonine to isoleucine at amino acid residue number 160, an amino acid substitution from alanine to threonine at amino acid residue number 173, an amino acid substitution from threonine to lysine at amino acid residue number 202, an amino acid substitution from glutamic acid to lysine at amino acid residue number 203, an amino acid substitution from threonine to isoleucine at amino acid residue number 231, an amino acid substitution from alanine to threonine at amino acid residue number 267, an amino acid substitution from asparagine to aspartic acid at amino acid residue number 279, an amino acid substitution from asparagine to aspartic acid at amino acid residue number 280, an amino acid substitution from glutamic acid to lysine at amino acid residue number 334, an amino acid substitution from glutamic acid to lysine at amino acid residue number 340, an amino acid substitution from asparagine to aspartic acid at amino acid residue number 391, an amino acid substitution from threonine to alanine at amino acid residue number 393, an amino acid substitution from glutamine to arginine at amino acid residue number 399, an amino acid substitution from valine to isoleucine at amino acid residue number 405, an amino acid substitution from valine to isoleucine at amino acid residue number 429, an amino acid substitution from glutamic acid to valine at amino acid residue number 437, an amino acid substitution from threonine to alanine at amino acid residue number 439, and an amino acid substitution from glycine to alanine at amino acid residue number 666, wherein the amino acid residue number of said compensatory mutation is relative to the amino acid sequence of parental HIV-2/vcp gp120 as provided in SEQ ID NO:5.

8. The isolated nucleic acid of claim 6, wherein said V3 deletion is Δ V3(6,6) and further wherein said compensatory mutation is at least one amino acid

substitution selected from the group consisting of an amino acid substitution from isoleucine to valine at amino acid residue number 55, an amino acid substitution from asparagine to aspartic acid at amino acid residue number 79, an amino acid substitution from threonine to lysine at amino acid residue number 202, an amino acid substitution from threonine to isoleucine at amino acid residue number 231, an amino acid substitution from alanine to threonine at amino acid residue number 267, and an amino acid substitution from asparagine to aspartic acid at amino acid residue number 391, wherein the amino acid residue number of said compensatory mutation is relative to the amino acid sequence of parental HIV-2/vcp gp120 as provided in SEQ ID NO:5.

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9. The isolated nucleic acid of claim 6, wherein said V3 deletion is $\Delta V3(6,6)$ and further wherein said compensatory mutation is at least one amino acid substitution selected from the group consisting of an amino acid substitution from isoleucine to valine at amino acid residue number 55, an amino acid substitution from asparagine to aspartic acid at amino acid residue number 79, an amino acid substitution from phenylalanine to serine at amino acid residue number 94, an amino acid substitution from asparagine to aspartic acid at amino acid residue number 280, and an amino acid substitution from asparagine to aspartic acid at amino acid residue number 391, wherein the amino acid residue number of said compensatory mutation is relative to the amino acid sequence of parental HIV-2/vcp gp120 as provided in SEQ ID NO:5.

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10. The isolated nucleic acid of claim 4, wherein said V3 deletion is $\Delta V3(6,6)$ and further wherein said compensatory mutation is at least one amino acid substitution selected from the group consisting of an amino acid substitution from threonine to alanine at amino acid residue number 393, and an amino acid substitution from valine to isoleucine at amino acid residue number 429, wherein the amino acid residue number of said compensatory mutation is relative to the amino acid sequence of parental HIV-2/vcp gp120 as provided in SEQ ID NO:5.

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11. The isolated nucleic acid of claim 6, wherein said V3 deletion is $\Delta V3(1,1)$ and further wherein said compensatory mutation is at least one of an amino

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acid substitution selected from the group consisting of an amino acid substitution from alanine to threonine at amino acid residue number 173, an amino acid substitution from glutamic acid to lysine at amino acid residue number 203, an amino acid substitution from threonine to alanine at amino acid residue number 393, an amino acid substitution
5 from glutamine to arginine at amino acid residue number 405, an amino acid substitution from valine to isoleucine at amino acid residue number 429, an amino acid substitution from threonine to alanine at amino acid residue number 439, and an amino acid substitution from glycine to alanine at amino acid residue number 666, wherein the amino acid residue number of said compensatory mutation is relative to the amino acid sequence
10 of parental HIV-2/vcp gp120 as provided in SEQ ID NO:5.

12. An isolated nucleic acid encoding a mammalian immunodeficiency virus glycoprotein (gp) 120 polypeptide, or a mutant, derivative, or fragment thereof, wherein said gp120 polypeptide comprises a deletion of hypervariable loop 3 (V3), a
15 deletion of hypervariable loops V1/V2, and further comprises a compensatory mutation wherein the nucleic acid sequence of said nucleic acid is selected from the group consisting of the sequence of SEQ ID NO:11, the sequence of SEQ ID NO:17, and the sequence of SEQ ID NO:29.

20 13. The isolated nucleic acid of claim 12, wherein said deletion is selected from the group consisting of a deletion from about amino acid residue number 303 to amino acid residue number 324 ($\Delta V3(6,6)$), and a deletion from about amino acid residue number 298 to amino acid residue number 331 ($\Delta V3(1,1)$), relative to the amino acid sequence of HIV-2/vcp gp120 as provided in SEQ ID NO:5.

25 14. An isolated nucleic acid encoding a mammalian immunodeficiency virus glycoprotein (gp) 120 polypeptide, or a mutant, derivative, or fragment thereof, wherein said gp120 polypeptide comprises a $\Delta V3(6,6)$ deletion, and further comprises a compensatory mutation wherein the nucleic acid sequence of said nucleic acid comprises
30 the sequence of SEQ ID NO:23.

15. The isolated nucleic acid of claim 1, wherein the sequence of said nucleic acid is at least one sequence selected from the group consisting of SEQ ID NO:8, SEQ ID NO:14, SEQ ID NO:20, and SEQ ID NO:26.

5 16. The isolated nucleic acid of claim 1, wherein the amino acid sequence of said gp120 polypeptide encoded by said nucleic acid is selected from the group consisting of the amino acid sequence of SEQ ID NO:11, the amino acid sequence of SEQ ID NO:17, the amino acid sequence of SEQ ID NO:23, and the amino acid sequence of SEQ ID NO:29.

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17. An isolated nucleic acid encoding a mammalian immunodeficiency virus gp41 polypeptide, wherein said gp41 polypeptide comprises a compensatory mutation.

15 18. The isolated nucleic acid of claim 17, wherein the nucleic acid sequence of said isolated nucleic acid is selected from the group consisting of the nucleic acid sequence of SEQ ID NO:9, the sequence of SEQ ID NO:15, the sequence of SEQ ID NO:21, and the sequence of SEQ ID NO:27.

20 19. The isolated nucleic acid of claim 17, wherein the amino acid sequence of said gp41 polypeptide encoded by said nucleic acid is selected from the group consisting of the amino acid sequence of SEQ ID NO:12, the amino acid sequence of SEQ ID NO:18, the amino acid sequence of SEQ ID NO:24, and the amino acid sequence of SEQ ID NO:30.

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20. The isolated nucleic acid of claim 17, wherein said compensatory mutation is a truncation of the cytoplasmic domain.

30 21. The isolated nucleic acid of claim 17, wherein said compensatory mutation is at least one mutation selected from the group consisting of an amino acid substitution from leucine to valine at amino acid residue number 518, an amino acid

substitution from alanine to threonine at amino acid residue number 529, an amino acid substitution from isoleucine to valine at amino acid residue number 531, an amino acid substitution from alanine to threonine at amino acid residue number 561, and an amino acid substitution from alanine to threonine at amino acid residue number 673, wherein the amino acid residue number of said compensatory mutation is relative to the amino acid sequence of HIV-2/vcp gp41 (SEQ ID NO:6).

22. The isolated nucleic acid of claim 20, wherein said truncation is selected from the group consisting of a truncation at amino acid residue number 733, a truncation at amino acid residue number 753, a truncation at amino acid residue number 764, wherein the amino acid residue number of said truncation is relative to the amino acid sequence of HIV-2/vcp gp41 (SEQ ID NO:6).

23. An isolated mammalian immunodeficiency virus gp120 polypeptide, wherein said polypeptide comprises a substantial deletion of V3 and further comprises a compensatory mutation.

24. The isolated polypeptide of claim 23, wherein said polypeptide is fusogenic.

25. The isolated gp120 polypeptide of claim 23, wherein said mammalian immunodeficiency virus is selected from the group consisting of a simian immunodeficiency virus (SIV), a human immunodeficiency virus type 1 (HIV-1), and a human immunodeficiency virus type 2 (HIV-2).

26. The isolated gp120 polypeptide of claim 25, wherein said mammalian immunodeficiency virus is HIV-2.

27. The isolated gp120 polypeptide of claim 26, wherein said deletion of V3 is selected from the group consisting of a deletion of from about amino acid residue number 303 to amino acid residue number 324 (Δ V3(6,6)) relative to the amino acid

sequence of HIV-2/vcp gp120 as provided in SEQ ID NO:5, and a deletion from about amino acid residue number 298 to amino acid residue number 331 ($\Delta V3(1,1)$) relative to the amino acid sequence of HIV-2/vcp gp120 as provided in SEQ ID NO:5.

5 28. The isolated gp120 polypeptide of claim 27, wherein said gp120 further comprises a deletion of the V1/V2 region.

 29. The isolated gp120 polypeptide of claim 28, wherein said compensatory mutation is at least one mutation selected from the group consisting of an
10 amino acid substitution from isoleucine to valine at amino acid residue number 55, an amino acid substitution from asparagine to aspartic acid at amino acid residue number 79, an amino acid substitution from phenylalanine to serine at amino acid residue number 94, an amino acid substitution from aspartic acid to glycine at amino acid residue number 142, an amino acid substitution from threonine to isoleucine at amino acid residue
15 number 160, an amino acid substitution from alanine to threonine at amino acid residue number 173, an amino acid substitution from threonine to lysine at amino acid residue number 202, an amino acid substitution from glutamic acid to lysine at amino acid residue number 203, an amino acid substitution from threonine to isoleucine at amino acid residue number 231, an amino acid substitution from alanine to threonine at amino
20 acid residue number 267, an amino acid substitution from asparagine to aspartic acid at amino acid residue number 279, an amino acid substitution from asparagine to aspartic acid at amino acid residue number 280, an amino acid substitution from glutamic acid to lysine at amino acid residue number 334, an amino acid substitution from glutamic acid to lysine at amino acid residue number 340, an amino acid substitution from asparagine
25 to aspartic acid at amino acid residue number 391, an amino acid substitution from threonine to alanine at amino acid residue number 393, an amino acid substitution from valine to isoleucine at amino acid residue number 399, an amino acid substitution from glutamine to arginine at amino acid residue number 405, an amino acid substitution from valine to isoleucine at amino acid residue number 429, an amino acid substitution from
30 glutamic acid to valine at amino acid residue number 437, an amino acid substitution from threonine to alanine at amino acid residue number 439, and an amino acid

substitution from glycine to alanine at amino acid residue number 666, wherein the amino acid residue number of said compensatory mutation is relative to the amino acid sequence of parental HIV-2/vcp gp120 as provided in SEQ ID NO:5.

5 30. The isolated gp120 polypeptide of claim 29, wherein said V3 deletion is $\Delta V3(6,6)$ and further wherein said compensatory mutation is at least one of an amino acid substitution selected from the group consisting of an amino acid substitution from isoleucine to valine at amino acid residue number 55, an amino acid substitution from asparagine to aspartic acid at amino acid residue number 79, an amino acid substitution
10 from threonine to lysine at amino acid residue number 202, an amino acid substitution from threonine to isoleucine at amino acid residue number 231, an amino acid substitution from alanine to threonine at amino acid residue number 267, and an amino acid substitution from asparagine to aspartic acid at amino acid residue number 391, wherein the amino acid residue number of said compensatory mutation is relative to the
15 amino acid sequence of parental HIV-2/vcp gp120 as provided in SEQ ID NO:5.

 31. The isolated gp120 polypeptide of claim 29, wherein said V3 deletion is $\Delta V3(6,6)$ and further wherein said compensatory mutation is at least one of an amino acid substitution selected from the group consisting of an amino acid substitution from
20 isoleucine to valine at amino acid residue number 55, an amino acid substitution from asparagine to aspartic acid at amino acid residue number 79, an amino acid substitution from phenylalanine to serine at amino acid residue number 94, an amino acid substitution from asparagine to aspartic acid at amino acid residue number 280, and an amino acid substitution from asparagine to aspartic acid at amino acid residue number 391, wherein
25 the amino acid residue number of said compensatory mutation is relative to the amino acid sequence of parental HIV-2/vcp gp120 as provided in SEQ ID NO:5.

 32. The isolated gp120 polypeptide of claim 27, wherein said V3 deletion is $\Delta V3(6,6)$ and further wherein said compensatory mutation is at least one of an
30 amino acid substitution selected from the group consisting of an amino acid substitution from threonine to alanine at amino acid residue number 393, and an amino acid

substitution from valine to isoleucine at amino acid residue number 429, wherein the amino acid residue number of said compensatory mutation is relative to the amino acid sequence of parental HIV-2/vcp gp120 as provided in SEQ ID NO:5.

5 33. The isolated gp120 polypeptide of claim 29, wherein said V3 deletion is $\Delta V3(1,1)$ and further wherein said compensatory mutation is at least one of an amino acid substitution selected from the group consisting of an amino acid substitution from alanine to threonine at amino acid residue number 173, an amino acid substitution from glutamic acid to lysine at amino acid residue number 203, an amino acid
10 substitution from threonine to alanine at amino acid residue number 393, an amino acid substitution from glutamine to arginine at amino acid residue number 405, an amino acid substitution from valine to isoleucine at amino acid residue number 429, an amino acid substitution from threonine to alanine at amino acid residue number 439, and an amino acid substitution from glycine to alanine at amino acid residue number 666, wherein the
15 amino acid residue number of said compensatory mutation is relative to the amino acid sequence of parental HIV-2/vcp gp120 as provided in SEQ ID NO:5.

 34. An isolated gp120 polypeptide, or a mutant, derivative, or fragment thereof, wherein said gp120 polypeptide comprises a deletion of hypervariable
20 loop 3 (V3), a deletion of hypervariable loops V1/V2, and further comprises a compensatory mutation wherein the amino acid sequence of said gp120 polypeptide is selected from the group consisting of the sequence of SEQ ID NO:11, the sequence of SEQ ID NO:17, and the sequence of SEQ ID NO:29.

25 35. An isolated gp120 polypeptide, or a mutant, derivative, or fragment thereof, wherein said gp120 polypeptide comprises a deletion of hypervariable loop 3 (V3), and further comprises a compensatory mutation wherein the amino acid sequence of said gp120 polypeptide comprises the sequence of SEQ ID NO:23.

30 36. An isolated mammalian immunodeficiency virus gp41 polypeptide, wherein said gp41 comprises a compensatory mutation.

37. The isolated gp41 polypeptide of claim 36, wherein said compensatory mutation is at least one mutation selected from the group consisting of an amino acid substitution from leucine to valine at amino acid residue number 518, an amino acid substitution from alanine to threonine at amino acid residue number 529, an amino acid substitution from isoleucine to valine at amino acid residue number 531, an amino acid substitution from alanine to threonine at amino acid residue number 561, and an amino acid substitution from alanine to threonine at amino acid residue number 673, wherein the amino acid residue number of said compensatory mutation is relative to the amino acid sequence of HIV-2/vcp gp41 (SEQ ID NO:6).

38. The isolated gp41 polypeptide of claim 36, wherein said compensatory mutation is a truncation of the cytoplasmic domain.

39. The isolated gp41 polypeptide of claim 38, wherein said truncation is selected from the group consisting of a truncation at amino acid 733, a truncation at amino acid 753, and a truncation at amino acid 764, wherein the amino acid residue number of said compensatory mutation is relative to the amino acid sequence of HIV-2/vcp gp41 (SEQ ID NO:6).

40. The isolated gp41 polypeptide of claim 36, wherein the amino acid sequence of said polypeptide is selected from the group consisting of the sequence of SEQ ID NO:12, the sequence of SEQ ID NO:18, the sequence of SEQ ID NO:24, and the sequence of SEQ ID NO:30.

41. A composition comprising a mammalian immunodeficiency virus gp120 polypeptide, wherein said gp120 polypeptide comprises a substantial deletion of V3, and a pharmaceutically acceptable carrier.

42. The composition of claim 41, said composition further comprising a mammalian immunodeficiency virus gp41 polypeptide, wherein said gp41 comprises a

compensatory mutation.

43. The composition of claim 42, wherein said gp120 further comprises a deletion of V1/V2.

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44. The composition of claim 43, wherein the amino acid sequence of said gp120 polypeptide comprises at least one sequence selected from the group consisting of the sequence of the sequence of SEQ ID NO:11, the sequence of SEQ ID NO:17, and the sequence of SEQ ID NO:29.

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45. The composition of claim 44, wherein the amino acid sequence of said gp41 polypeptide comprises at least one sequence selected from the group consisting of the sequence of the sequence of SEQ ID NO:12, the sequence of SEQ ID NO:18, and the sequence of SEQ ID NO:30.

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46. The composition of claim 42, wherein the amino acid sequence of said gp120 polypeptide comprises at least one sequence selected from the group consisting of the sequence of the sequence of SEQ ID NO:11, the sequence of SEQ ID NO:17, the sequence of SEQ ID NO:23, and the sequence of SEQ ID NO:29.

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47. The composition of claim 46, wherein the amino acid sequence of said gp41 polypeptide comprises at least one sequence selected from the group consisting of the sequence of the sequence of SEQ ID NO:12, the sequence of SEQ ID NO:18, the sequence of SEQ ID NO:24, and the sequence of SEQ ID NO:30.

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48. An isolated mammalian immunodeficiency virus, said virus comprising a gp120 polypeptide wherein said gp120 comprises a substantial deletion of V3.

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49. The isolated virus of claim 48, wherein said virus is fusion-competent.

50. The isolated virus of claim 49, wherein said virus is replication-competent.

51. The isolated virus of claim 50, said virus further comprising a gp41 polypeptide wherein said gp41 comprises a compensatory mutation.

52. The isolated virus of claim 50, wherein said gp120 polypeptide comprises a compensatory mutation.

53. The isolated virus of claim 52, wherein the amino acid sequence of said gp120 polypeptide comprises at least one sequence selected from the group consisting of the sequence of the sequence of SEQ ID NO:11, the sequence of SEQ ID NO:17, the sequence of SEQ ID NO:23, and the sequence of SEQ ID NO:29.

54. The isolated virus of claim 53, wherein the amino acid sequence of said gp41 polypeptide comprises at least one sequence selected from the group consisting of the sequence of the sequence of SEQ ID NO:12, the sequence of SEQ ID NO:18, the sequence of SEQ ID NO:24, and the sequence of SEQ ID NO:30.

55. An isolated mammalian immunodeficiency virus Env, wherein said Env comprises a substantial deletion of V3 and further wherein said Env is fusogenic.

56. The isolated mammalian immunodeficiency virus Env of claim 55, wherein the amino acid sequence of said Env comprises at least one sequence selected from the group consisting of the sequence of SEQ ID NO:10, the sequence of SEQ ID NO:16, the sequence of SEQ ID NO:22, and the sequence of SEQ ID NO:28.

57. A method of producing a neutralizing antibody in a mammal in need thereof, said method comprising administering to a mammal an immunogenic amount of an isolated gp120, wherein said gp120 comprises a substantial deletion of V3, and further comprises a deletion of V1/V2, thereby producing said neutralizing antibody in said

mammal.

58. The method of claim 57, wherein the amino acid sequence of said isolated gp120 comprises at least one sequence selected from the group consisting of the sequence of SEQ ID NO:11, the sequence of SEQ ID NO:17, the sequence of SEQ ID NO:23, and the sequence of SEQ ID NO:29.

59. The method of claim 57, wherein said gp120 further comprises a deletion of V4.

60. A method of eliciting a neutralizing antibody in a mammal, said method comprising administering an immunogenic amount of the composition of claim 43, thereby eliciting said neutralizing antibody in said mammal.

61. The method of claim 60, wherein said mammal is selected from the group consisting of an ape, and a human.

62. An antibody produced by the method of claim 60.

63. An antibody elicited by the method of claim 57.

64. A method of producing a replication-competent mammalian immunodeficiency virus comprising a deletion of at least one hypervariable loop domain, said method comprising

a) producing a virus comprising gp120 wherein said gp120 comprises a deletion of V1/V2, said gp120 further comprising a substantial deletion of V3;

b) passaging said virus in cell culture and selecting for a virus that is capable of fusing with a cell;

c) introducing into said virus selected in (b) a gp41 comprising enhanced fusogenicity wherein said gp41 comprises at least one compensatory mutation; and

d) passaging the virus of (c) in cell culture and selecting for a virus that is

capable of fusing with a cell;
thereby producing said replication-competent virus.

65. A replication-competent virus produced by the method of claim 64.

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66. A method of identifying a determinant of a chemokine receptor that specifically binds with a gp120 polypeptide of a mammalian immunodeficiency virus, said method comprising contacting a high-affinity gp120 polypeptide of said virus with a panel of mutants of said chemokine receptor, assessing the binding of said gp120
10 polypeptide with each of said mutants, and comparing said binding of said gp120 with each of said mutants, thereby identifying said determinant of said chemokine receptor that specifically binds with said gp120.

67. A method of identifying a compound that inhibits binding of a
15 mammalian immunodeficiency virus gp120 polypeptide with a chemokine receptor, said method comprising assessing the level of binding of a gp120 polypeptide comprising a deletion of V1/V2, and a substantial deletion of V3, wherein said gp120 is fusogenic, with a chemokine receptor in the presence of a compound, and comparing the level of binding of said gp120 with said chemokine receptor in the presence of said compound
20 with the binding of an otherwise identical gp120 with an otherwise identical chemokine receptor in the absence of said compound, wherein a lower level of binding of said gp120 with said chemokine receptor in the presence of said compound compared with the level of binding of said otherwise identical gp120 with said otherwise identical chemokine receptor in the absence of said compound is an indication that said compound inhibits
25 binding of said gp120 with said chemokine receptor, thereby identifying a compound that inhibits binding of said gp120 with said chemokine receptor.

68. A kit for producing an immunodeficiency virus-neutralizing antibody in a mammal, said kit comprising an immunogenic amount of a gp120 polypeptide of
30 said mammalian immunodeficiency virus, wherein said gp120 comprises a deletion of V1/V2, and a substantial deletion of V3, said kit further comprising an applicator, and an

instructional material for the use thereof.

69. The kit of claim 68, wherein the amino acid sequence of said gp120 polypeptide is at least one sequence selected from the group consisting of group
5 consisting of the sequence of SEQ ID NO:11, the sequence of SEQ ID NO:17, the sequence of SEQ ID NO:23, and the sequence of SEQ ID NO:29.

70. A kit for producing an immunodeficiency virus-neutralizing antibody in a mammal, said kit comprising an immunogenic amount of a mammalian
10 immunodeficiency virus Env, wherein said Env comprises a deletion of V1/V2, and a substantial deletion of V3, and further wherein said Env comprises a compensatory mutation, said kit further comprising an applicator, and an instructional material for the use thereof.

15 71. The kit of claim 70, wherein the amino acid sequence of said Env comprises at least one sequence selected from the group consisting of the sequence of SEQ ID NO:10, the sequence of SEQ ID NO:16, the sequence of SEQ ID NO:22, and the sequence of SEQ ID NO:28.

20 72. A kit for eliciting a neutralizing antibody in a mammal, said kit comprising an immunogenic amount of the composition of claim 43, said kit further comprising an applicator, and an instructional material for the use thereof.